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| EXAMINER |
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ALSTRUM ACEVEDO, JAMES HENRY

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| ART UNIT | PAPER NUMBER |
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1616

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10/26/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/820,656

Applicant(s)

GONG ET AL.

Examiner

James H. Alstrum-Acevedo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29, 32-33, 36-37, and 40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 29, 32-33, 36-37, and 40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 29, 32-33, 36-37, and 40 are pending. Applicants previously cancelled original claims 1-28. Applicants have newly cancelled claims 30-31, 34-35, 38-39, and 41-52. Applicants have amended claims 32 and 36. Receipt and consideration of Applicants' remarks/arguments and amended claim set submitted on August 31, 2007 are acknowledged.

Moot Rejections/objections

All rejections and/or objections of claims 30-31, 34-35, 38-39, and 41-52 cited in the previous office action mailed on April 13, 2007 **are moot**, because said claims /have been cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 32 and 36 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) **is maintained** for the reasons of record set forth in the office action mailed on April 13, 2007. Additionally it is noted that (1) the pressure value of "between 40 and 60 psi" in claims 32 and 36 lacks written support in the specification, because the only pressures mentioned in the specification are 40 psi and 60 psi in paragraph [0064] and there is no support for a range of pressure values.

Response to Arguments

Applicant's arguments filed August 13, 2007 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that (1) because the specification's disclosure of a pressure of 40 psi for one study and a pressure of 60 psi for another separate study is alleged as providing ample support because an ordinary skilled artisan would expect reasonable activity between 40 and 60 psi; (2) similarly a temperature range of "between 60 °C and 70 °C" is also allegedly supported because an ordinary skilled artisan would expect reasonable activity in this temperature range; (3) Applicants' amendments to recite relative humidity instead of humidity in claims 32 and 36 has overcome this aspect of the instant rejection.

The Examiner respectfully disagrees with Applicants' traversal arguments (1) and (2). Applicants' specification does not set forth a range of pressures or temperatures over which the claimed method is practiced. Rather, Applicants' specification only recites two individual points for the spray drying pressure (i.e. 40 psi or 60 psi) and two temperatures for spray drying (i.e. 60 °C and 70°C). The support for these two different pressure and temperature values is found in paragraph [0064], which describes two different studies that do not imply a range of temperatures or pressures, but merely two independent and distinct points. Applicants have also requested the Examiner provide evidence to support the position that these points are not adequately described such that an ordinary skilled artisan would not expect reasonable activity. Additional support for this rejection is not believed necessary, because the instant rejection concerns written description not enablement. Thus, whereas the method is enabled, it is deemed to lack adequate written description, as described above and in the office action mailed on April 13, 2007.

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Regarding the new matter concerning a flow rate of “approximately 18 standard cubic feet per minute (scfm),” Applicants’ amendment to recite a flow rate of “approximately 17.8” does not remove the new matter. As set forth in the April 2007 office action the only flow rate point having support in the specification is a value of 17.8 scfm, which although similar, does not support values of approximately 17.8 scfm or 18 scfm.

Regarding (3), Applicants’ claim amendments to recite relative humidity has overcome this facet of the new matter rejection. In summary, claims 32 and 36 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

The rejection of claims 29, 32-33, 36 and 40 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is maintained** for the reasons of record set forth in the April 13, 2007 office action. It is noted that Applicants have not traversed the instant rejection or amended the claims to remove the indefinite language; thus, it is deemed to remain proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

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the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 29, 33, 37, 40 under 35 U.S.C. 103(a) as being unpatentable over Lechuga-Ballesteros et al. (WO 01/32144) in view of Kurachi et al. (*Blood Coagulation and Fibrinolysis*, 1993; ("Kurachi")) **is maintained** for the reasons of record set forth on pages 4-7 of the office action mailed on February 21, 2006 and further articulated on page 5 of the office action mailed on July 27, 2006.

Response to Arguments

Applicant's arguments filed April 13, 2007 have been fully considered but they are not persuasive. Applicants' traversal arguments are based on their assertions that (1) Kurachi is irrelevant, because the structure of F.IX in vivo is nothing like the claimed environment (dry powder); (2) the formulations of Applicants' claimed method and those taught by Lechuga are not identical and thus, would not have the same or substantially similar properties; (3) allegedly inherent properties are not necessarily present in the method and composition suggested by the prior art; (4) obviousness cannot be predicated on what is unknown; (5) Applicants have allegedly shown unexpected results, because inhalation of F.IX provides a significant and surprising improvement over intravenous F.IX; (6) nebulization of protein solutions creates shear that would be expected to denature proteins; (7) the Examiner has allegedly not provided any "competent" evidence; and (8) Lechuga allegedly fails to provide a reasonable expectation of success.

The Examiner respectfully disagrees with Applicants' traversal arguments. Regarding (1), Kurachi is relevant, because it demonstrates that Factor IX (F.IX) is single

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polypeptide (i.e. monomeric), thus the F.IX utilized by Lechuga is monomeric. Applicants have not provided any credible evidence that Lechuga's dry powder formulations comprising F.IX are not monomeric. It is noted that the method of producing dry powders described by Lechuga is the essentially the same as that taught by Applicants (i.e. use of aqueous solutions and drying to keep water content below 10% w/w). Thus, an ordinary skilled artisan would reasonably conclude that the F.IX dry powders produced by Lechuga is monomeric.

Regarding (2)-(3), Applicants' claimed methods do not specify the composition of the dry powder that is aerosolized in the claimed method, but merely physical properties upon aerosolization of said dry powder and that the powder have less than 10% w/w water. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a first inhalable dry powder comprising (a) 32.6% F.IX, (b) 7.4% sodium citrate, and (c) 60% leucine or a second inhalable dry powder comprising (a) 52.6% F.IX, 7.4% sodium citrate, and 40% trileucine) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Because the aerodynamic properties (e.g. MMAD and FPF) taught by Lechuga are essentially the same as those taught by Applicants, Lechuga's F.IX dry powders are deemed to have the same properties as the powder utilized by Applicants in the claimed method (see Lechuga Example 7 on pages 44-45, especially Table 15 on page 44).

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Regarding (4), as far as can be determined from the prior art the dry powder F.IX formulations taught by Lechuga are substantially the same as those utilized by Applicants in the claimed methods. In Applicants' arguments, Applicants pointed out that their animal studies utilized formulations, which were not identical to the closest formulations taught by Lechuga. The primary difference between the formulations highlighted by Applicants in their application compared to those exemplified by Lechuga is the amount of F.IX present and the amount of sodium citrate utilized. Regarding the amount of F.IX, the difference in amounts between the prior art's (37% and 56%) and Applicants' exemplified compositions (32.6% and 52.6%) was 3.4% w/w. However, there is no evidence in Applicants' specification to indicate that there is any criticality regarding the presence of F.IX in an amount of 32.6% w/w or 52.6% w/w. No correlation between the claimed aerodynamic values and physiological observations of inhaling F.IX. powder comprising 32.6% w/w or 52.6% w/w is evident from Applicants' data. Concerning the amount of sodium citrate, there is no indication from Applicants' data in the specification that it is critical for the compositions to comprise 7.4% sodium citrate to exhibit the claimed aerodynamic properties and physiological "depot" effects. Applicants' data also do not suggest or demonstrate that the depot effect is dependent on any particular amount of F.IX, sodium citrate, or combination thereof. Thus, given that the prior art compositions is essentially the same as Applicants' compositions utilized in the claimed methods, it is concluded that it is reasonably expected that the prior art compositions upon administration by inhalation would exhibit the same depot effect (the prior art compositions demonstrate the same aerodynamic properties).

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Applicants' argument (5) is off point. Lechuga does not suggest or teach the intravenous administration of Factor IX, but rather teaches *inhalable Factor IX dry powders*. Thus, the Examiner does not understand Applicants arguments as to why the difference between intravenous administration of Factor IX is relevant to overcoming the prima facie obviousness case based upon the teachings of Lechuga suggesting the inhalation administration of Factor IX dry powders. Similarly, argument (6) concerning the problems associated with the nebulization of aqueous solutions of proteins (e.g. Factor IX) are irrelevant with regards to the suggested method of Lechuga, wherein dry powders comprising Factor IX are inhaled. If Applicants were suggesting that inhalation of Factor IX dry powders would also result in shear that would denature Factor IX, then this would also be a characteristic of Applicants claimed method, which aerosolizes Factor IX dry powder. Finally, regarding (7)-(8) and rebutted arguments (1)-(6), it is concluded that the instant rejection remains proper, because the competent evidence (i.e. the teachings of the prior art) has clearly been set forth on the record.

The rejection of claims 32 and 36 under 35 U.S.C. 103(a) as being unpatentable over Lechuga in view of Kurachi as applied to claims 29-31, 33-35, and 37-42 above, and further in view of Huang et al. (U.S. Patent No. 6,280,729; "Huang") **is maintained** for the reasons of record and articulated above in the instant office action.

Response to Arguments

Applicant's arguments filed April 13, 2007 have been fully considered but they are not persuasive. Applicants' traversal arguments are presumed to be the same as those

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that were addressed above in the instant office action. The rebuttal to these arguments is incorporated herein by reference and the instant rejection is deemed to remain proper.

Conclusion

Claims 29, 32-33, 36-37, and 40 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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